

● PRINTER RUSH ●

(PTO ASSISTANCE)

TFW

Application: <u>09635364</u>	Examiner: <u>CANELLA</u>	GAU: <u>1642</u>
From: <u>TF</u>	Location: <u>IDC</u> FMF FDC	Date: <u>8-23-05</u>

Tracking #: 5991812 Week Date: 8-9-05

DOC CODE	DOC DATE	MISCELLANEOUS
<input type="checkbox"/> 1449	_____	<input type="checkbox"/> Continuing Data
<input type="checkbox"/> IDS	_____	<input checked="" type="checkbox"/> Foreign Priority
<input type="checkbox"/> CLM	_____	<input type="checkbox"/> Document Legibility
<input type="checkbox"/> IIFW	_____	<input type="checkbox"/> Fees
<input type="checkbox"/> SRFW	_____	<input type="checkbox"/> Other
<input type="checkbox"/> DRW	_____	
<input type="checkbox"/> OATH	_____	
<input type="checkbox"/> 312	_____	
<input type="checkbox"/> SPEC	_____	

[RUSH] MESSAGE: A 35 U.S.C. 119(a)-(d)
foreign priority claim cannot
be based on a U.S. application.
Please make all necessary corrections
to file wrapper & specifications.
See MPEP 1293.03(c) priority under
35 U.S.C. 120.
Thank you

[XRUSH] RESPONSE: A PCT application can be used as a
foreign priority document. Please see the attached examples
of recently issued patents: US 6,884,771, US 6,887,974,
US 6,855,559, US 6,800,604, US 6,790,624.

INITIALS: KAL

NOTE: This form will be included as part of the official USPTO record, with the Response document coded as XRUSH.
 REV 10/04



US006884771B1

(12) **United States Patent**
Acton et al.

(10) **Patent No.:** **US 6,884,771 B1**
(45) Date of Patent: **Apr. 26, 2005**

(54) **ANGIOTENSIN CONVERTING ENZYME
HOMOLOG AND USES THEREFOR**

(75) **Inventors:** Susan Acton, Lexington, MA (US);
Keith E. Robison, Wilmington, MA
(US); Frank Y. Hsieh, Lexington, MA
(US)

(73) **Assignee:** Millennium Pharmaceuticals, Inc.,
Cambridge, MA (US)

(*) **Notice:** Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 472 days.

(21) **Appl. No.:** 09/635,501

(22) **Filed:** Aug. 9, 2000

Related U.S. Application Data

(63) Continuation-in-part of application No. 09/407,427, filed on
Sep. 29, 1999, which is a continuation-in-part of application
No. 09/163,648, filed on Sep. 30, 1998, which is a continu-
ation-in-part of application No. 08/989,299, filed on Dec. 11,
1997.

(30) **Foreign Application Priority Data**

Sep. 29, 1999 (WO) PCT/US99/22976

(51) **Int. Cl.⁷** A51K 38/00

(52) **U.S. Cl.** 514/2; 514/12; 530/350;
530/361; 424/94.1; 424/94.6; 435/183;
435/195

(58) **Field of Search** 514/2, 12; 530/350,
530/361; 424/94.1, 94.6; 435/183, 195;
536/23.5; 800/7

(56) **References Cited**

FOREIGN PATENT DOCUMENTS

EP 0 974 664 A2 1/2000
WO WO 00/18899 A2 A3 4/2000

OTHER PUBLICATIONS

DGENE Accession No. AAY 84562 for "A human angio-
tensin converting enzyme-2 (ACE-2) protein," Jul. 25,
2000.

DGENE Accession No. AAA12764 for "cDNA encoding a
human angiotensin converting enzyme-2 (ACE-2)," Jul. 25,
2000.

DGENE Accession No. AAY67310 for "Human MPROT15
amino acid sequence #1," Apr. 11, 2000.

DGENE Accession No. AAZ59465 for "Human MPROT15
coding sequence #1," Apr. 11, 2000.

EMBL Accession No. AF241254 for "*Homo sapiens* angio-
tensin converting enzyme-like protein mRNA, complete
cds," Jul. 1, 2000.

SWALL Accession No. Q9NRA7 for "Angiotensin convert-
ing enzyme-like protein (ACE-related carboxypeptidase
ACE2)," Oct. 1, 2000.

Bernstein, K. E. "Two ACEs and a heart," *Nature* Jun. 20,
2002; 417:799,801-802.

Donoghue, M. et al. "A novel angiotensin-converting
enzyme-related carboxypeptidase (ACE2) converts angio-
tensin I to angiotensin 1-9," *Circulation Research* Sep. 1,
2000; 87(5):e1-e9.

Tipnis, S.R. et al. "A human homolog of angiotensin-con-
verting enzyme. Cloning and functional expression as a
captopril-insensitive carboxypeptidase," *Journal of Biologi-
cal Chemistry* Oct. 27, 2000; 275(43):33238-33243.

Primary Examiner—Christopher R. Tate

Assistant Examiner—B. Dell Chism

(74) *Attorney, Agent, or Firm*—Millennium
Pharmaceuticals, Inc.

(57) **ABSTRACT**

The present invention relates to the discovery of novel genes
encoding an angiotensin converting enzyme, Angiotensin
Converting Enzyme-2 (ACE-2). The invention provides
therapeutics, prognostic and diagnostics methods for treat-
ing blood pressure related disorders as well as various types
of allergic conditions, among others. Also disclosed are
screening assays for identifying compounds for treating and
preventing these conditions.

25 Claims, 23 Drawing Sheets



US006887974B2

(12) **United States Patent**
Pathak(10) **Patent No.:** **US 6,887,974 B2**
(45) **Date of Patent:** **May 3, 2005**(54) **CROSSLINKING AGENTS AND METHODS OF USE**(75) **Inventor:** **Chandrashekhar P. Pathak, Austin, TX (US)**(73) **Assignee:** **Incept LLC, Lexington, MA (US)**(*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 421 days.(21) **Appl. No.:** **10/068,807**(22) **Filed:** **Feb. 5, 2002**(65) **Prior Publication Data**

US 2002/0114775 A1 Aug. 22, 2002

Related U.S. Application Data

(62) Division of application No. 09/147,897, filed on Aug. 30, 1999.

(60) Provisional application No. 60/026,526, filed on Sep. 23, 1996, provisional application No. 60/039,904, filed on Mar. 4, 1997, and provisional application No. 60/040,417, filed on Mar. 13, 1997.

(30) **Foreign Application Priority Data**

Sep. 22, 1997 (WO) PCT/US97/16897

(51) **Int. Cl.⁷** **C09F 15/00; C08G 63/48; C08G 63/08**(52) **U.S. Cl.** **530/200; 530/350; 530/380; 530/382; 525/54.1; 525/54.11; 525/54.2; 528/354; 528/361**(58) **Field of Search** **530/200, 350, 530/380, 382; 525/54.1, 54.11, 54.2; 528/354, 361**(56) **References Cited****U.S. PATENT DOCUMENTS**

2,533,004 A 12/1950 Ferry et al. 640/82
 3,520,949 A 7/1970 Shepard et al. 604/164
 4,101,380 A * 7/1978 Rubinstein et al. 435/181
 4,359,049 A 11/1982 Redl et al. 128/218
 4,565,784 A 1/1986 Franzblau et al. 435/240
 4,601,286 A 7/1986 Kaufman 128/999,989
 4,631,055 A 12/1986 Redl et al. 604/82
 4,646,730 A 3/1987 Schonfeld et al. 999/156
 4,670,417 A 6/1987 Iwasaki et al. 514/6
 4,735,616 A 4/1988 Eibl et al. 604/191
 4,874,368 A 10/1989 Miller et al. 604/82
 4,902,281 A 2/1990 Avoy 604/191
 4,932,942 A 6/1990 Maslanka 604/164
 4,937,270 A 6/1990 Hamilton et al. 514/777
 4,938,763 A 7/1990 Dunn et al. 604/891.1
 4,978,336 A 12/1990 Capozzi et al. 604/82
 5,024,742 A 6/1991 Nesburn et al. 204/157.68
 5,030,215 A 7/1991 Morse et al. 604/410
 5,041,292 A 8/1991 Feijen 424/484
 5,104,909 A 4/1992 Grasel 521/159
 5,116,315 A 5/1992 Capozzi et al. 604/82
 5,143,662 A 9/1992 Chesterfield 264/8
 5,162,430 A 11/1992 Rhee et al. 525/54.1
 5,192,743 A 3/1993 Hsu et al. 514/8

5,296,518 A 3/1994 Grasel 521/176
 5,304,595 A 4/1994 Rhee et al. 525/54.1
 5,318,524 A 6/1994 Morse et al. 604/82
 5,324,775 A 6/1994 Rhee et al. 525/54.2
 5,328,955 A 7/1994 Rhee et al. 525/54.1
 5,368,563 A 11/1994 Lonneman et al. 604/82
 5,395,923 A 3/1995 Bui-Khac et al. 530/381
 5,399,351 A 3/1995 Leshchiner et al. 424/422
 5,405,607 A 4/1995 Epstein 424/94.64
 5,410,016 A * 4/1995 Hubbell et al. 528/354
 5,413,791 A 5/1995 Rhee et al. 424/422
 5,419,491 A 5/1995 Breitsprecher 239/9
 5,426,148 A 6/1995 Tucker 524/496
 5,446,090 A 8/1995 Harris 525/54.1
 5,446,091 A 8/1995 Rhee et al. 525/54.1
 5,455,027 A 10/1995 Zalipsky et al.
 5,470,911 A 11/1995 Rhee et al. 525/54.1
 5,474,540 A 12/1995 Miller et al. 604/191
 5,475,052 A 12/1995 Rhee et al. 525/54.1
 5,476,909 A 12/1995 Kim et al. 525/408
 5,505,704 A 4/1996 Pawelka et al. 604/191
 5,514,379 A 5/1996 Weissleder et al. 424/426
 5,514,380 A 5/1996 Song et al. 424/426
 5,527,856 A 6/1996 Rhee et al. 525/54.1
 5,529,914 A 6/1996 Hubbell et al. 435/182
 5,550,187 A 8/1996 Rhee et al. 525/54.1
 5,565,519 A 10/1996 Rhee et al. 525/54.1
 5,567,435 A 10/1996 Hubbell et al. 424/426

(Continued)

FOREIGN PATENT DOCUMENTS

EP 0557199 8/1993
 WO WO 91/09641 7/1991
 WO WO 94/03155 2/1994

(Continued)

OTHER PUBLICATIONS

US 6,214,374, 4/2001, Schmirler et al. (withdrawn)
 Kissell et al., "Parenteral depot-systems on the basis of biodegradable polyesters", *J of Controlled Release* 16:27-42 (1991).

(Continued)

Primary Examiner—Jon Weber**Assistant Examiner**—Abdel A. Mohamed(74) **Attorney, Agent, or Firm**—Patterson, Thunte, Skaar & Christensen, P.A.(57) **ABSTRACT**

Polymeric crosslinking agents are disclosed that have an inert water soluble polymeric component, biodegradable components, functional components reactive with chemical groups on a protein, for example, amine or thiol groups. The inert polymeric component may be flanked at each end with a biodegradable component which is flanked at each end with a protein reactive functional component. A polymeric crosslinking agent is disclosed having a biodegradable component, polyalkylene oxide, and at least three reactive functional groups that are each capable of forming a covalent bond in water with at least one functional group such as an amine, thiol, or carboxylic acid.

25 Claims, 7 Drawing Sheets



US00685559B1

(12) **United States Patent**
Christensen et al.

(10) Patent No.: **US 6,855,559 B1**
(45) Date of Patent: **Feb. 15, 2005**

(54) **REMOVAL OF EMBEDDING MEDIA FROM BIOLOGICAL SAMPLES AND CELL CONDITIONING ON AUTOMATED STAINING INSTRUMENTS**

(75) Inventors: **Kimberly Christensen**, Tucson, AZ (US); **Ethel R. Macrea**, Tucson, AZ (US); **Noemi Sebastiao**, Tucson, AZ (US)

4,888,998 A 12/1989 Buzza et al.
5,023,187 A 6/1991 Koebler et al.
5,075,079 A 12/1991 Kerr et al.
5,187,099 A 2/1993 Healy, Jr. Stephen F. et al.
5,244,787 A 9/1993 Key et al.
5,273,905 A 12/1993 Muller et al.
5,318,795 A 6/1994 Stokes et al.

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

(73) Assignee: **Ventana Medical Systems, Inc.**, Tucson, AZ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 81 days.

CA	1059744 A	* 8/1979 C09K/7/02
CN	1279273	1/2001	
EP	0508568	10/1992	
WO	93/09486	5/1993	
WO	94/04906	3/1994	
WO	9524498	9/1995	
WO	0188500	11/2001	

OTHER PUBLICATIONS

Protocol "Ziehl-Neelsen stain fr AFB" <http://medlib.med.utah.edu/WebPath/HISTHTML/MANUALS/ZIEHL.PDF>, Aug. 03, 1999.*

(List continued on next page.)

Related U.S. Application Data

(60) Provisional application No. 60/099,018, filed on Sep. 3, 1998.

Foreign Application Priority Data

Feb. 26, 1999 (WO) PCT/US99/04181
Sep. 3, 1999 (WO) PCT/US99/20353

(51) Int. Cl.⁷ **G01N 1/18**

(52) U.S. Cl. **436/177; 436/174; 436/175; 436/139**

(58) Field of Search **436/139, 174-177; 422/61, 100, 58; 427/2.11; 455/40.52, 40.5**

References Cited

U.S. PATENT DOCUMENTS

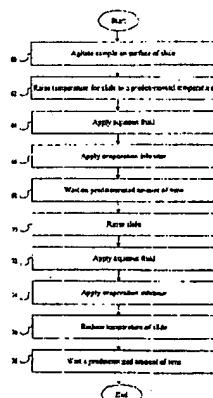
4,043,292 A 8/1977 Rogers et al.
4,384,193 A 5/1983 Kledzik et al.
4,543,236 A 9/1985 von Gise
4,629,862 A 12/1986 Kitagawa et al.
4,644,807 A 2/1987 Mar
4,746,491 A 5/1988 Ohlin
4,858,155 A 8/1989 Okawa et al.
4,865,986 A 9/1989 Coy et al.

Primary Examiner—Yelena G. Gakh
(74) *Attorney, Agent, or Firm*—McDonnell Boehnen Hulbert & Berghoff LLP

(57) ABSTRACT

The present invention provides reagents for use in an automated environment for removing or etching embedding media by exposing a biological sample to be stained in histochemical or cytochemical procedures without the dependence on organic solvents. The reagents comprise components optimized to facilitate removal or etching of the embedding media from the biological sample. The present invention also provides reagents for use in an automated environment for cell conditioning biological samples wherein the cells are predisposed for access by reagent molecules for histochemical and cytochemical staining procedures. The reagents comprise components optimized to facilitate molecular access to cells and cell constituents within the biological sample.

16 Claims, 8 Drawing Sheets





US006800604B2

(12) **United States Patent**
Gurney et al.

(10) Patent No.: **US 6,800,604 B2**
(45) Date of Patent: **Oct. 5, 2004**

(54) **POLYPEPTIDES THAT INHIBIT HUMAN
SERUM-INDUCED CLEAVAGE OF
HEPATOCTE GROWTH FACTOR**

(75) Inventors: **Austin L. Gurney**, Belmont, CA (US);
Daniel K. Kirchhofer, Los Altos, CA
(US); **William I. Wood**, Hillsborough,
CA (US)

(73) Assignee: **Genentech, Inc.**, South San Francisco,
CA (US)

(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 105 days.

(21) Appl. No.: **09/742,201**

(22) Filed: **Dec. 19, 2000**

(65) **Prior Publication Data**

US 2002/0123091 A1 Sep. 5, 2002

Related U.S. Application Data

(60) Provisional application No. 60/253,665, filed on Nov. 28,
2000.

(30) **Foreign Application Priority Data**

Feb. 11, 2000 (WO) PCT/US00/03565
Mar. 15, 2000 (WO) PCT/US00/06884

(51) Int. Cl.⁷ **C07K 14/00; A61K 38/00**

(52) U.S. Cl. **514/2; 530/300; 530/350;**
514/12; 424/85.1; 424/198.1

(58) Field of Search **530/300, 350,**
530/351; 514/2, 12; 424/85.1, 184.1, 192.1,
198.1

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,736,866 A 4/1988 Leder et al.
4,873,191 A 10/1989 Wagner et al.
5,573,762 A 11/1996 Ferrara et al.
5,610,134 A 3/1997 Clark et al.
5,624,806 A 4/1997 Baker et al.
5,650,282 A 7/1997 Keating et al.
5,661,122 A 8/1997 Clark et al.
5,773,223 A 6/1998 Shyamala et al.
5,773,414 A 6/1998 Cody et al.
5,935,924 A 8/1999 Bunting et al.

FOREIGN PATENT DOCUMENTS

EP 0 759 467 A 2/1997
WO 97/12629 4/1997
WO 01/05972 A1 1/2001

OTHER PUBLICATIONS

Falkenberg et al. Expression of a functional proteinase
inhibitor capable of accepting xylose: bikunin. Arch Bio-
chem Biophys 387(1):99-106, 2001.*

Kataoka et al. Hepatocyte growth factor activator inhibitor
type 1 is a specific cell surface binding protein of hepatocyte
growth factor activator (HGFA) and regulates HGFA activ-
ity in the pericellular microenvironment. J Biol Chem
275(51):40453-40462, 2000.*

Hamasuna et al. Reduced expression of hepatocyte growth
factor activator inhibitor type-2/placental bikunin (HAI-2/
PB) in human glioblastomas: implication for anti-invasive
role of HAI-2/PB in glioblastoma cells. Int J Cancer 93:
339-3435, 2001.*

Adamis et al., "Inhibition of Vascular Endothelial Growth
Factor Prevents Retinal Ischemia-Associated Iris Neovas-
cularization in a Nonhuman Primate" Arch. Ophthalmology
114(1):66-71 (1996).

Aiello et al., "Vascular endothelial growth factor in ocular
fluid of patients with diabetic retinopathy and other retinal
disorders" New England J. of Medicine 331(22):1480-1487
(1994).

Berkman et al., "Expression of the vascular permeability
factor/vascular endothelial growth factor gene in central
nervous system neoplasms" J. Clin. Invest. 91(1):153-159
(1993).

Betocchi et al., "Effects of Diltiazem on left ventricular
systolic and diastolic function in hypertrophic cardiomyopa-
thy" Am. J. Cardiol. 78:451-457 (1996).

Boznak, M. Can. J. Biochem. Physiol. 33:985-994 (1955).

Bonow et al., "Verapamil-induced improvement in left
ventricular diastolic filling and increased exercise tolerance
in patients with hypertrophic cardiomyopathy: short- and
long-term effects" Circulation 72:853-864 (1985).

Borgstrom et al., "Complete inhibition of angiogenesis and
growth of microtumors by anti-vascular endothelial growth
factor neutralizing antibody: novel concepts of angiostatic
therapy from intravital videomicroscopy" Cancer Research
56(17):4032-4039 (1996).

(List continued on next page.)

Primary Examiner—Elizabeth Kemmerer

Assistant Examiner—Bridget E. Bunner

(74) Attorney, Agent, or Firm—Paul Naik; Craig Svoboda

(57)

ABSTRACT

Compositions and methods are disclosed for stimulating or
inhibiting angiogenesis and/or cardiovascularization in
mammals, including humans. Pharmaceutical compositions
are based on polypeptides or antagonists thereto that have
been identified for one or more of these uses. Disorders that
can be diagnosed, prevented, or treated by the compositions
herein include trauma such as wounds, various cancers, and
disorders of the vessels including atherosclerosis and cardiac
hypertrophy. In addition, the present invention is directed to
novel polypeptides and to nucleic acid molecules encoding
those polypeptides. Also provided herein are vectors and
host cell comprising those nucleic acid sequences, chimeric
polypeptide molecules comprising the polypeptides of the
present invention fused to heterologous polypeptide
sequences, antibodies which bind to the polypeptides of the
present invention and to methods for producing the polypep-
tides of the present invention.

27 Claims, 5 Drawing Sheets



US006790624B2

(12) **United States Patent**
Mayer

(10) **Patent No.:** US 6,790,624 B2
(45) **Date of Patent:** Sep. 14, 2004

(54) **COILED-COIL MEDIATED
HETERODIMERIZATION FUNCTIONAL
INTERACTION TRAP**

(75) **Inventor:** Bruce J. Mayer, Tolland, CT (US)

(73) **Assignee:** The University of Connecticut,
Farmington, CT (US)

(*) **Notice:** Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 238 days.

(21) **Appl. No.:** 09/816,756

(22) **Filed:** Mar. 24, 2001

(65) **Prior Publication Data**

US 2002/0037999 A1 Mar. 28, 2002

Related U.S. Application Data

(60) Provisional application No. 60/141,896, filed on Jun. 30,
1999.

(30) **Foreign Application Priority Data**

Jun. 29, 2000 (WO) PCT/US00/17929

(51) **Int. Cl.⁷** G01N 33/53

(52) **U.S. Cl.** 435/7.1; 435/6; 435/5;
435/4; 530/350; 536/23.4

(58) **Field of Search** 435/7.1, 6, 5, 4;
530/350; 324; 536/23.4

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,270,964 B1 * 8/2001 Michnick et al. 435/6

FOREIGN PATENT DOCUMENTS

WO	WO 00/07038	2/2000
WO	WO 01/00866	1/2001

OTHER PUBLICATIONS

Tripet et al, Protein Engineering, 9, (11), 1029-1042
(1996).*

H. Hurst, Transcription Factors 1: bZIP Proteins, Protein
Profile, 1995, vol. 2, Issue 2, pp. 105-168.

M. Tanaka, et al., Differential Inhibition of Signaling Path-
ways by Dominant-Negative SH2/SH3 Adapter Proteins,
Molecular and Cellular Biology, Dec. 1995, vol. 15, No. 12,
pp. 6829-6837.

R. Hodges, De Novo Design of α -helical Proteins: Basic
Research to Medical Applications, Biochemistry and Cell
Biology, 1996, vol. 74, No. 2, pp. 133-154.

Y. Mizukami, et al., Plant Organ Size Control: AINTEGU-
MENTA Regulates Growth and Cell Numbers During Orga-
nogenesis, PNAS, Jan. 18, 2000, vol. 97, No. 2, pp.
942-947.

K. Arndt, et al., Heterodimeric Coiled-Coil Peptide Pair
Selected in Vivo From A Designed Library-Versus-Library
Ensemble, Journal of Molecular Biology, 2000, vol. 295, pp.
627-639.

2 Hybrid System TRAF0 Protocol, <http://www.umanitoba.ca/faculties/medicine/biochem/gietz/2HS.html>.

Mammalian Two-Hybrid Assay Kit, http://www.stratagene.com/vectors/signal_trans/mam2hyb.htm.

Display Green Two-Hybrid Kit System, http://www.displaysystems.com/Prod...displaygreen_two-hybrid_kit_sy.htm.

A Iivanainen, Coiled-Coil Motif in Proteins, <http://www.wpi.edu/dept/chem-eng/Biotech-Envirom/Ryan/cc.html>.

Coiled-Coil Motifs are Formed, <http://bmbiris.bmb.uga.edu/wampler/8010/lectures/motifs/sld018.htm>.

Coiled Coil, <http://www-class.unl.edu/bios201/chapter2cWEB/sld024.htm>.

Some Common Protein Motifs; <http://bioag.byu.edu/mcbio/130/proteinfuction/sld018.html>.

The Structure of a Coiled Coil; <http://bioag.byu.edu/mcbio/130/proteinfuction/sld019.html>.

Coiled-Coil Structures; http://www.microbio.uab.edu/Seq-Course/08_Protein/sld043.html.

PPT Slide; http://www.microbio.uab.edu/SeqCourse/08_Protein/sld045.html.

New Twists in Globes and Zippers; <http://www.psc.edu/science/Brooks96/brooks96/html>, pp. 1-3.

Prediction of Coiled Coils from Protein Sequences; <http://www.york.ac.uk/depts/biol/units/coils/coilcoil.html>.

Structural Classification of Proteins, Class: Coiled Coil
Proteins; <http://www.edu.au/scop/data/scop.1.008.html>.

GAL4 (Residues 1-65); ftp://www.expasy.ch/databases/swiss-3dimage/IMAGES/JPEG/1D66_gal4_1.jpg.

Motifs; http://mytilene.ucdavis.edu/~smith...ir/Protein_Structure_II/sld017.html; Slides 2, and 17-29.

Posttranslational Modifications; http://mytilene.ucdavis.edu/~smith...r/Protein_Structure_III/sld001.html; Slides 1-6, 10 and 26.

Influenza Virus Haemagglutinin, <http://www.rpi.edu/dept/chem-eng/Biotech-Envirom/Ryan/cc.html>, pp. 4-5.

* cited by examiner

Primary Examiner—T. D. Wessendorf

(74) **Attorney, Agent, or Firm**—McCarter & English LLP

(57) **ABSTRACT**

Fusion proteins containing coiled-coil heterodimerization domains substituted for modular protein binding domains useful for validating functionally relevant protein-protein interactions, directing enzymes to specific substrates, and screening fusion libraries for functionally important interaction partners.

2 Claims, 3 Drawing Sheets